

? b-155,357

05may03 09:43:18 User208669 Session D2276.1

\$0.32 0.093 DialUnits File1

\$3.32 Estimated cost File1

\$0.01 TELNET

\$0.33 Estimated cost this search

\$0.33 Estimated total session cost 0.093 DialUnits

SYSTEM:OS - DIALOG OneSearch

File 155:MEDLINE(R) 1966-2003/Apr W4

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\*File 155: Medline has been reloaded and accession numbers have

changed. Please see HELP NEWS 155.

File 357:Derwent Biotech Res. 1982-2003/Apr W4

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\*File 357: File is now current. See HELP NEWS 357.

Alert feature enhanced for multiple files, etc. See HELP ALERT.

# Set Items Description

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? ds

Set Items Description

S1 10344905 PY<1999

S2 0 SECOND(3N)BOOST?

S3 222 SECOND(3N)BOOST?

S4 164 S1 AND S3

S5 158957 VECTOR OR VECTORS

S6 7 S4 AND S5

S7 165 DIFFERENT(W)VECTORS

S8 108 S1 AND S7

S9 103 RD (unique items)

S10 700069 IMMUNE OR IMMUNO? OR VACCINE?

S11 14 S9 AND S10

S12 119 THREE (3N) S5 AND S10

S13 42 S12 AND S1

? t s6/7/1-6

6/7/1 (Item 1 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

(c) format only 2003 The Dialog Corp. All rts. reserv.

11365461 98246107 PMID: 9586695

A vector DNA vaccine encoding pseudorabies virus immediate early protein

demonstrates partial protection in mice against lethal virus challenge.

Chang S W; Bu J; Rompato G; Garmendia A E

Department of Pathobiology, University of Connecticut, Storrs 06269, USA.

Viral immunology (UNITED STATES) 1998, 11 (1) p27-36, ISSN

0882-8245 Journal Code: 8801552

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

An earlier study in our laboratory provided evidence that pseudorabies virus (PrV) immediate early protein (IE180) may contribute to the overall immune response against PrV. To examine the response by IE180 more closely, we initiated a vaccine trial in mice with a vector DNA construct that contains the gene encoding for IE180, designated pcDNAIE180. The DNA vaccine was delivered in gold microcarriers using a Helios Gene Gun, and 70% of BALB/c mice given the DNA vaccine (2 microg/mouse) seroconverted within 2 weeks. The remaining negative mice seroconverted after a single vaccine booster. Essentially similar results were obtained on vaccination of C57BL/6 mice, whereas C3H/HeJ mice remained negative after the first vaccination, but responded after a booster. Seven months after immunization with pcDNAIE180, an overall 25% of BALB/c, C3H/HeJ, and C57BL/6 mice receiving a lethal PrV challenge were protected. In addition, a significant passive transfer of IE180-specific antibodies to the offspring from pregnant mice vaccinated with pcDNAIE180 was observed. Interestingly, a moderate level of protection (27.6%) was also observed when these offspring received a lethal PrV challenge. Moreover, an enhancement of immune responses and a twofold increase in the level of protection were observed in mice that received a second vaccine booster by gene gun 8 months after the first vaccination. Together, these data support the theory that IE180 may indeed play a role in the overall protective immunity against PrV.

Record Date Created: 19980624

Record Date Completed: 19980624

6/7/2 (Item 2 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

(c) format only 2003 The Dialog Corp. All rts. reserv.

11127323 98001376 PMID: 9343211

An adenovirus-simian immunodeficiency virus env vaccine elicits humoral,

cellular, and mucosal immune responses in rhesus macaques and decreases

viral burden following vaginal challenge.

Buge S L; Richardson E; Alipanah S; Markham P; Cheng S; Kalyan N; Miller

C J; Lubeck M; Udem S; Eldridge J; Robert-Guroff M

Basic Research Laboratory, National Cancer Institute, Bethesda, Maryland

20892, USA.

Journal of virology (UNITED STATES) Nov 1997, 71 (11) p8531-41,

ISSN 0022-538X Journal Code: 0113724

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Six female rhesus macaques were immunized orally and intranasally at 0 weeks and intratracheally at 12 weeks with an adenovirus type 5 host range mutant (Ad5lr)-simian immunodeficiency virus SIVsm env recombinant and at

24 and 36 weeks with native SIVmac251 gp120 in Syntex adjuvant. Four macaques received the Ad5hr vector and adjuvant alone; two additional controls were naive. In vivo replication of the Ad5hr wild-type and recombinant vectors occurred with detection of Ad5 DNA in stool samples and/or nasal secretions in all macaques and increases in Ad5 neutralizing antibody in 9 of 10 macaques following Ad administrations. SIV-specific neutralizing antibodies appeared after the second recombinant immunization and rose to titers > 10,000 following the second subunit boost. Immunoglobulin G (IgG) and IgA antibodies able to bind gp120 developed in nasal and rectal secretions, and SIV-specific IgGs were also observed in vaginal secretions and saliva. T-cell proliferative responses to SIV gp140 and T-helper epitopes were sporadically detected in all immunized macaques. Following vaginal challenge with SIVmac251, transient or persistent infection resulted in both immunized and control monkeys. The mean viral burden in persistently infected immunized macaques was significantly decreased in the primary infection period compared to that of control macaques. These results establish in vivo use of the Ad5hr vector, which overcomes the host range restriction of human Ads for rhesus macaques, thereby providing a new model for evaluation of Ad-based vaccines. In addition, they show that a vaccine regimen using the Ad5hr-SIV env recombinant and gp120 subunit induces strong humoral, cellular, and mucosal immunity in rhesus macaques. The reduced viral burden achieved solely with an env-based vaccine supports further development of Ad-based vaccines comprising additional viral components for immune therapy and AIDS vaccine development.

Record Date Created: 19971113

Record Date Completed: 19971113

6/7/3 (Item 3 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

(c) format only 2003 The Dialog Corp. All rts. reserv.

10862509 97213974 PMID: 9060663

Humoral, mucosal, and cellular immunity in response to a human immunodeficiency virus type 1 immunogen expressed by a Venezuelan equine encephalitis virus vaccine vector.

Caley I J; Betts M R; Irlbeck D M; Davis N L; Swanstrom R; Frelinger J A; Johnston R E

Department of Microbiology, School of Medicine, University of North Carolina, Chapel Hill 27599, USA.

Journal of virology (UNITED STATES) Apr 1997, 71 (4) p3031-8, ISSN 0022-538X Journal Code: 0113724

Contract/Grant No.: 5-T32-AI07273-12; AI; NIAID

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

A molecularly cloned attenuated strain of Venezuelan equine encephalitis

virus (VEE) has been genetically configured as a replication-competent vaccine vector for the expression of heterologous viral proteins (N. L. Davis, K. W. Brown, and R. E. Johnston, J. Virol. 70:3781-3787, 1996). The matrix/capsid (MA/CA) coding domain of human immunodeficiency virus type 1 (HIV-1) was cloned into the VEE vector to determine the ability of a VEE vector to stimulate an anti-HIV immune response in mice. The VEE-MA/CA vector replicated rapidly in the cytoplasm of baby hamster kidney (BHK) cells and expressed large quantities of antigenically identifiable MA/CA protein. When injected subcutaneously into BALB/c mice, the vector invaded and replicated in the draining lymphoid tissues, expressing HIV-1 MA/CA at a site of potent immune activity. Anti-MA/CA immunoglobulin G (IgG) and IgA antibodies were present in serum of all immunized mice, and titers increased after a second booster inoculation. IgA antibodies specific for MA/CA were detected in vaginal washes of mice that received two subcutaneous immunizations. Cytotoxic T-lymphocyte responses specific for MA/CA were detected following immunization with the MA/CA-expressing VEE vector. These findings demonstrate the ability of a VEE-based vaccine vector system to stimulate a comprehensive humoral and cellular immune response. The multifaceted nature of this response makes VEE an attractive vaccine for immunization against virus infections such as HIV-1, for which the correlates of protective immunity remain unclear, but may include multiple components of the immune system.

Record Date Created: 19970411

Record Date Completed: 19970411

6/7/4 (Item 4 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

(c) format only 2003 The Dialog Corp. All rts. reserv.

10651901 97000549 PMID: 8843634

DNA-mediated immunization to hepatitis B surface antigen: longevity of primary response and effect of boost.

Davis H L; Mancini M; Michel M L; Whalen R G

Loeb Medical Research Institute, Ottawa Civic Hospital, Canada.

Vaccine (ENGLAND) Jun 1996, 14 (9) p910-5, ISSN 0264-410X

Journal Code: 8406899

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Intramuscular (i.m.) injection of mice with plasmid DNA expression vectors containing all or part of the hepatitis B virus (HBV) gene encoding the envelope proteins induces a strong humoral response to the HBV surface antigen (HBsAg) which is sustained for up to 74 weeks without boost. After a single i.m. injection of 100 micrograms DNA, antibodies to HBsAg (anti-HBs) reach ELISA titers of 4 x 10(4) in C57BL/6 mice and 10(4) in BALB/c mice, or somewhat less in older mice. Although antibody levels induced by a single injection of DNA do not diminish significantly over

time, they can be further increased 10-200-fold by boosting with a second injection of DNA or an injection of recombinant HBsAg protein. Prior injection of DNA does not affect the strength or timing of the boosting effect, suggesting that there is no immune response against the vector itself. Boosting with a second injection of DNA is possible even in BALB/c mice, which are known to have a strong cytotoxic T-lymphocyte response against an epitope on the major HBV envelope protein, indicating that possible destruction of newly transfected muscle fibers is not so quick and efficient as to abort the boosting effect. A single injection of DNA results in a stronger and longer lasting humoral response than does a single injection of recombinant protein.  
Record Date Created: 19970205  
Record Date Completed: 19970205

6/7/5 (Item 5 from file: 155)  
DIALOG(R)File 155:MEDLINE(R)  
(c) format only 2003 The Dialog Corp. All rts. reserv.  
08617614 95306141 PMID: 7598771  
A prime-boost approach to HIV preventive vaccine using a recombinant canarypox virus expressing glycoprotein 160 (MN) followed by a recombinant glycoprotein 160 (MN/LAI). The AGIS Group, and l'Agence Nationale de Recherche sur le SIDA.  
Pialoux G; Excler J L; Riviere Y; Gonzalez-Canali G; Feuille V; Coulaud P; Gluckman J C; Matthews T J; Meignier B; Kieny M P, et al  
Hopital de l'Institut Pasteur, Paris, France.  
AIDS research and human retroviruses (UNITED STATES) Mar 1995, 11 (3) p373-81, ISSN 0889-2229 Journal Code: 8709376  
Erratum in AIDS Res Hum Retroviruses 1995 Jul;11(7) 875  
Document type: Clinical Trial; Journal Article; Multicenter Study; Randomized Controlled Trial  
Languages: ENGLISH  
Main Citation Owner: NLM  
Record type: Completed

The safety and the immunogenicity of a recombinant canarypox live vector expressing the human immunodeficiency virus type 1 (HIV-1) gp160 gene from the MN isolate, ALVAC-HIV (vCP125), followed by booster injections of a soluble recombinant hybrid envelope glycoprotein MN/LAI (rgp160), were evaluated in vaccinia-immune, healthy adults at low risk for acquiring HIV-1 infection. Volunteers (n = 20) received vCP125 (10(6) TCID50) at 0 and 1 month, followed randomly by rgp160 formulated in alum or in Freund's incomplete adjuvant (FIA) at 3 and 6 months. Local and systemic reactions were mild or moderate and resolved within the first 72 hr after immunization. No significant biological changes in routine tests were observed in any volunteer. Two injections of vCP125 did not elicit antibodies. Neutralizing antibodies (NA) against the HIV-1 MN isolate were detected in 65 and 90% of the subjects after the first and the second rgp160 booster injections, respectively. Six months after the last boost, only

55% were still positive. Seven of 14 sera with the highest NA titers against MN weakly cross-neutralized the HIV-1 SF2 isolate; none had NA against the HIV-1 LAI or against a North American primary isolate. Specific lymphocyte T cell proliferation to rgp160 was detected in 25% of the subjects after vCP125 and in all subjects after the first booster injection and 12 months after the first injection. An envelope-specific cytotoxic lymphocyte activity was found in 39% of the volunteers and characterized for some of them as CD3+, CD8+, MHC class I restricted. The adjuvant formulation did not influence significantly the immune responses (ABSTRACT TRUNCATED AT 250 WORDS)  
Record Date Created: 19950727  
Record Date Completed: 19950727

6/7/6 (Item 6 from file: 155)  
DIALOG(R)File 155:MEDLINE(R)  
(c) format only 2003 The Dialog Corp. All rts. reserv.  
05834377 88188233 PMID: 2833606  
Immunization with a vaccinia virus recombinant expressing herpes simplex virus type 1 glycoprotein D: long-term protection and effect of revaccination.  
Rooney J F; Wohlenberg C; Cremer K J; Moss B; Notkins A L  
Laboratory of Oral Medicine, National Institute of Dental Research, Bethesda, Maryland 20892.  
Journal of virology (UNITED STATES) May 1988, 62 (5) p1530-4, ISSN 0022-538X Journal Code: 0113724  
Document type: Journal Article  
Languages: ENGLISH  
Main Citation Owner: NLM  
Record type: Completed  
Previously we showed that mice immunized with a vaccinia virus vector expressing the herpes simplex virus type 1 (HSV-1) glycoprotein D (gD) gene (vaccinia/gD) were protected against both lethal and latent infections with HSV-1 for at least 6 weeks after immunization (K. J. Cremer, M. Mackett, C. Wohlenberg, A. L. Notkins, and B. Moss, Science 228:737-740, 1985). In the experiments described here, we examined long-term immunity to HSV following vaccinia/gD vaccination, the effect of revaccination with vaccinia/gD, and the impact of previous immunity to vaccinia virus on immunization with the gD recombinant. Mice immunized with vaccinia/gD showed 100, 100, and 80% protection against lethal infection with HSV-1 at 18, 44, and 60 weeks postimmunization, respectively. Protection against latent trigeminal ganglionic infection was 70, 50, and 31% at 6, 41, and 60 weeks postvaccination, respectively. To study the effect of reinimmunization on antibody levels, mice vaccinated with vaccinia/gD were given a second immunization (booster dose) 3 months after the first. These mice developed a 10-fold increase in neutralizing-antibody titer (221 to 2,934) and demonstrated a significant increase in protection against lethal HSV-1 challenge compared with animals that received only one dose of vaccinia/gD.

To determine whether preexisting immunity to vaccinia virus inhibited the response to vaccination with vaccinia/gD virus, mice were immunized with a recombinant vaccinia virus vector expressing antigens from either influenza A or hepatitis B virus and were then immunized (2 to 3 months later) with vaccinia/gD. These mice showed reduced titers of neutralizing antibody to HSV-1 and decreased protection against both lethal and latent infections with HSV-1 compared with animals vaccinated only with vaccinia/gD. We conclude that vaccination with vaccinia/gD produces immunity against HSV-1 that lasts over 1 year and that this immunity can be increased by a booster but that prior immunization with a vaccinia recombinant virus expressing a non-HSV gene reduces the levels of neutralizing antibody and protective immunity against HSV-1 challenge.

Record Date Created: 19880526

Record Date Completed: 19880526

? t sl17/2 7 9 20 13

11/7/2 (Item 2 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

(c) format only 2003 The Dialog Corp. All rts. reserv.

11150513 98026480 PMID: 9362157

Enhancing efficacy of recombinant anticancer vaccines with prime/boost regimens that use two different vectors.

Irvine K R; Chamberlain R S; Shulman E P; Surman D R; Rosenberg S A; Restifo N P

Surgery Branch, Division of Clinical Sciences, National Cancer Institute, Bethesda, MD 20892-1502, USA.

Journal of the National Cancer Institute (UNITED STATES) Nov 5 1997, 89 (21) p1595-601, ISSN 0027-8874 Journal Code: 7503089

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

**BACKGROUND:** The identification of tumor-associated antigens and the cloning of DNA sequences encoding them have enabled the development of anticancer vaccines. Such vaccines target tumors by stimulating an immune response against the antigens. One method of vaccination involves the delivery of antigen-encoding DNA sequences, and a number of recombinant vectors have been used for this purpose. To optimize the efficacy of recombinant vaccines, we compared primary and booster treatment regimens that used a single vector (i.e., homologous boosting) with regimens that used two different vectors (i.e., heterologous boosting). **METHODS:** Pulmonary tumors (experimental metastases) were induced in BALB/c mice inoculated with CT26.CL25 murine colon carcinoma cells, which express recombinant bacterial beta-galactosidase (the model antigen). Protocols for subsequent vaccination used three vectors that encoded beta-galactosidase--vaccinia (cowpox) virus, fowlpox virus, naked bacterial plasmid DNA. Mouse survival was evaluated in conjunction with antibody and cytotoxic T-lymphocyte responses to beta-galactosidase. **RESULTS:**

Heterologous boosting resulted in significantly longer mouse survival than homologous boosting (all  $P < 0.001$ , two-sided). Potent antigen-specific cytotoxic T lymphocytes were generated following heterologous boosting with poxvirus vectors. This response was not observed with any of the homologous boosting regimens. Mice primed with recombinant poxvirus vectors generated highly specific antibodies against viral proteins. **CONCLUSIONS:** The poor efficacy of homologous boosting regimens with viral vectors was probably a consequence of the induction of a strong antiviral antibody response. Heterologous boosting augmented antitumor immunity by generating a strong antigen-specific cytotoxic T-lymphocyte response. These data suggest that heterologous boosting strategies may be useful in increasing the efficacy of recombinant DNA anticancer vaccines that have now entered clinical trials.

Record Date Created: 19971125

Record Date Completed: 19971125

11/7/7 (Item 1 from file: 357)

DIALOG(R)File 357:Derwent Biotech Res.

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0219374 DBR Accession No.: 98-00971

Increasing efficacy of recombinant anticancer vaccines with prime/boost regimens that use two different vectors - heterologous, homologous booster injection regime comparison using vaccinia virus, fowl-pox virus, bacterium naked nucleic acid vaccine; potential in cancer gene therapy

AUTHOR: Irvine K R; Chamberlain R S; Shulman E P; Surman D R; Rosenberg S A; +Restifo N P

CORPORATE AFFILIATE: Nat. Cancer Inst. Bethesda

CORPORATE SOURCE: National Institutes of Health, Bldg. 10, R2B54, Bethesda, MD 20892-1502, USA.

JOURNAL: J.Natl.Cancer Inst. (89, 21 1595-600) 1997

ISSN: 0027-8874 CODEN: JNCIEQ

LANGUAGE: English

**ABSTRACT:** Anticancer vaccines target tumors by stimulating an immune response against the antigens. One method of vaccination involves the delivery of antigen-encoding DNA sequences, and a number of recombinant vectors have been used for this purpose. To optimize the efficacy of recombinant vaccines, primary and booster treatment regimens were compared that used 2 different vectors (i.e. heterologous boosting). Pulmonary tumors were induced in BALB/c mice inoculated with CT26.CL25 mouse colon carcinoma cells, which express recombinant bacterial beta-galactosidase (BG; model antigen). Protocols for subsequent vaccination used 3 vectors that encoded BG (vaccinia (cowpox) virus, fowl-pox virus, naked bacterial plasmid DNA. Mouse survival was evaluated in conjunction with antibody and cytotoxic T-lymphocyte responses to BG. Heterologous boosting resulted in significantly longer mouse survival than homologous boosting. This strategy may be useful in

increasing efficacy of recombinant DNA anticancer vaccines that have now entered clinical trials. (11 ref)

11/7/9 (Item 3 from file: 357)

DIALOG(R)File 357:Derwent Biotech Res.

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0187638 DBR Accession No.: 95-15153

Gene therapy - a novel form of drug delivery - gene transfer by retro virus, adeno virus, liposome and animal model

AUTHOR: Blau H M; Springer M L

CORPORATE AFFILIATE: Univ.Stanford

CORPORATE SOURCE: Department of Molecular Pharmacology, Stanford University School of Medicine, Stanford, CA 94305-5332, USA.

JOURNAL: N.Engl.J.Med. (333, 18, 1204-07) 1995

ISSN: 0028-4793 CODEN: NEJMAG

LANGUAGE: English

ABSTRACT: An overview of gene therapy, including the targets of gene therapy is discussed. Clinical evidence of gene therapy over the past 5 years has shown that in most cases, toxicity is not a problem. It is suggested that clinical tests of gene therapies may no longer require special consideration by the Recombinant DNA Advisory Committee to be performed, but should require the same rigorous evaluation as other novel medical treatments. Most gene therapy methods have involved the use of viruses as carriers of the gene, the carrier may be a retro virus or an adeno virus. Liposomes may also be used for gene transfer. Direct injection of naked DNA plasmids is possible, but this method only functions in heart and skeletal muscle. A potential desirable vector could be completely synthetic, a composite of DNA-sequence components derived from a number of existing viral and plasmid vectors. Some desirable properties may include the ability to incorporate large gene, the absence of immunogenicity and the potential to direct the vector to certain cell populations. Animal models of human genetic diseases have been used for testing and comparing different vectors for gene delivery. (0 ref)

? t s 11/7/10 13

11/7/10 (Item 4 from file: 357)

DIALOG(R)File 357:Derwent Biotech Res.

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0179677 DBR Accession No.: 95-07697

Use of a human immunodeficiency virus type-1 rev mutant without nucleolar dysfunction as a candidate for potential AIDS therapy - HIV virus mutant Rev protein gene cloning in a retro virus-based vector

AUTHOR: Furuta R A; Kubota S; Maki M; Miyazaki Y; Hattori T; +Hatanaka M

CORPORATE AFFILIATE: Univ.Kyoto-Inst. Virus-Res. Nat.Cancer-Inst.Frederick

CORPORATE SOURCE: Department of Molecular Virology, Institute for Virus Research, Kyoto University, Kyoto 606, Japan.

JOURNAL: J.Virol. (69, 3, 1591-99) 1995

ISSN: 0022-538X CODEN: JOVIAM

LANGUAGE: English

ABSTRACT: Applications of transdominant mutants of HIV virus-1 regulatory proteins, especially Rev, have been attempted for gene therapy against AIDS since the Rev protein is essential for viral replication. A mutant Rev protein (dRev) gene, drev, lacking the nucleolar targeting signal, was introduced into CD4-positive HeLa cells and human T-lymphocyte CCRF-CEM cells by 2 different vectors: plasmid pLdrev, a retro virus-based vector the drev cDNA under the control of the HIV 5' and 3' long terminal repeat regions; and plasmid pCdrev, with the drev cDNA under the control of the cytomegalo virus (CMV) promoter.

dRev-expressing HeLa cells transduced with the retro virus vector showed suppressed virus replication, syncytium formation and cell death caused by HIV-1 infection. The same vector conferred a similar phenotype on the CEM cells, and production was also suppressed in these cells containing the drev gene driven by the CMV promoter. Since dRev cannot migrate into the nuclei, it is expected not to interfere with nuclear/nucleolar functions of the host cell, and is a promising candidate as an antiviral molecule for AIDS gene therapy. (49 ref)

11/7/13 (Item 7 from file: 357)

DIALOG(R)File 357:Derwent Biotech Res.

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0131870 DBR Accession No.: 92-04362

Expression of Eimeria acervulina antigen in E. coli, Salmonella and fowlpox and the effect of immunization in chickens - Ea1a antigen partial gene cloning and expression in Escherichia coli, Salmonella gallinarum and fowl pox virus; potential recombinant vaccine; cross-protection (conference abstract)

AUTHOR: van den Boogaart; Vermeulen A N; Panhuyzen J; Groenink A; Kok H J; Tomley F M

CORPORATE AFFILIATE: Organon Intervet

CORPORATE SOURCE: Organon Int. BV, Department of Biochemistry and Biotechnology, P.O. Box 20, 5340 BH Oss, The Netherlands.

JOURNAL: J.Cell.Biochem. (Suppl.16A, 142) 1992

CODEN: JCEBD5

LANGUAGE: English

ABSTRACT: The Eimeria acervulina-derived antigen Ea1A (1269 bp open reading frame, partial gene) was cloned in different vectors. Escherichia coli MC1061 was transformed with plasmid pMLB1113(his), and produced a fusion protein with a 23-amino acid N-terminal leader which contained 6 His residues to facilitate purification by chelate affinity chromatography. Different E. coli-derived plasmids were tested using Salmonella gallinarum 9R as a host. Plasmid pMLB1113(his) demonstrated good expression in Salmonella, although quantitatively less than in E. coli. For expression in fowlpox virus, the Ea1A gene was fused to the

N-terminal signal peptide of the Newcastle-disease virus HN protein. The fusion protein was synthesized as an 81 kDa unit. Immunization of fowl with either a fusion protein subunit or the vectors resulted in moderate protection against *E. acervulina*, with 30-70% reduction in oocyst output. The Ea1a antigen has a homologous counterpart in *Eimeria tenella*, and cross-protection was found against lesion scores caused by *E. tenella*. Other species will be tested after the full gene has been cloned. (0 ref)

?ts137/9 10 13 33 40

137/9 (Item 9 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

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11150513 98026480 PMID: 9362157

Enhancing efficacy of recombinant anticancer vaccines with prime/boost regimens that use two different vectors.

Irvine K R; Chamberlain R S; Shulman E P; Surman D R; Rosenberg S A; Restifo N P

Surgery Branch, Division of Clinical Sciences, National Cancer Institute, Bethesda, MD 20892-1502, USA.

Journal of the National Cancer Institute (UNITED STATES) Nov 5 1997, 89 (21) p1595-601, ISSN 0027-8874 Journal Code: 7503089

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

BACKGROUND: The identification of tumor-associated antigens and the cloning of DNA sequences encoding them have enabled the development of anticancer vaccines. Such vaccines target tumors by stimulating an immune response against the antigens. One method of vaccination involves the delivery of antigen-encoding DNA sequences, and a number of recombinant vectors have been used for this purpose. To optimize the efficacy of recombinant vaccines, we compared primary and booster treatment regimens that used a single vector (i.e., homologous boosting) with regimens that used two different vectors (i.e., heterologous boosting). METHODS: Pulmonary tumors (experimental metastases) were induced in BALB/c mice inoculated with CT26.CL25 murine colon carcinoma cells, which express recombinant bacterial beta-galactosidase (the model antigen). Protocols for subsequent vaccination used three vectors that encoded beta-galactosidase--vaccinia (cowpox) virus, fowlpox virus, naked bacterial plasmid DNA. Mouse survival was evaluated in conjunction with antibody and cytotoxic T-lymphocyte responses to beta-galactosidase. RESULTS: Heterologous boosting resulted in significantly longer mouse survival than homologous boosting (all  $P < 0.0001$ , two-sided). Potent antigen-specific cytotoxic T lymphocytes were generated following heterologous boosting with poxvirus vectors. This response was not observed with any of the homologous boosting regimens. Mice primed with recombinant poxvirus vectors generated highly specific antibodies against viral proteins. CONCLUSIONS: The poor

efficacy of homologous boosting regimens with viral vectors was probably a consequence of the induction of a strong antiviral antibody response. Heterologous boosting augmented antitumor immunity by generating a strong antigen-specific cytotoxic T-lymphocyte response. These data suggest that heterologous boosting strategies may be useful in increasing the efficacy of recombinant DNA anticancer vaccines that have now entered clinical trials.

Record Date Created: 19971125

Record Date Completed: 19971125

137/10 (Item 10 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

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10979578 97332364 PMID: 9188598

Characterization of humoral and CD4+ cellular responses after genetic immunization with retroviral vectors expressing different forms of the hepatitis B virus core and e antigens.

Sallberg M; Townsend K; Chen M; O'Dea J; Banks T; Jolly D J; Chang S M; Lee W T; Milich D R

Department of Molecular Biology, Scripps Research Institute, La Jolla, California 92037, USA. masa@vird01.hs.sll.se

Journal of virology (UNITED STATES) Jul 1997, 71 (7) p5295-303, ISSN 0022-538X Journal Code: 0113724

Contract/Grant No.: AI20720; AI; NIAID; AI33562; AI; NIAID

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

The humoral and CD4+ cellular immune responses in mice following genetic immunization with three retroviral vectors encoding different forms of hepatitis B virus core antigen (HBcAg) and e antigen (HBcAg) were analyzed. The retroviral vectors induced expression of intracellular HBcAg (HBc[3A4]), secreted HBcAg (HBc[5A2]), or an intracellular HBcAg-neomycin phosphoryltransferase fusion protein (HBc-NEO[6A3]). Specific antibody levels and immunoglobulin G isotype restriction were highly dependent on both the host major histocompatibility complex and the transferred gene. Humoral and CD4+ cellular HBcAg and/or HBcAg (HBc/eAg)-specific immune responses following retroviral vector immunization were of a lower magnitude but followed the same characteristics compared with those after immunization with HBc/eAg in adjuvant. Two factors influenced the humoral responses. First, in vivo depletion of CD8+ cells in HBc-NEO[6A3]-immunized H-2k mice abrogated both HBcAg-specific antibodies and in vitro-detectable cytotoxic T lymphocytes. Second, priming of H-2b mice with an HBc/eAg-derived T-helper (Th) peptide in adjuvant prior to retroviral vector immunization greatly enhanced the HBc/eAg-specific humoral responses to all three vectors, suggesting that insufficient HBc/eAg-specific CD4+ Th-cell priming limits the humoral responses. In conclusion, direct

injection of retroviral vectors seems to be effective in priming HBc/eAg-specific CD8+ but comparatively inefficient in priming CD4+ Th cells and subsequently specific antibodies. However, the limited HBc/eAg-specific CD4+ cell priming can effectively be circumvented by prior administration of a recombinant or synthetic form of HBc/eAg in adjuvant.

Record Date Created: 19970710

Record Date Completed: 19970710

137/13 (Item 13 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

(c) format only 2003 The Dialog Corp. All rts. reserv.

10862511 97213976 PMID: 9060665

Multigene antiviral vectors inhibit diverse human immunodeficiency virus type 1 clades.

Gervais A; Li X; Kraus G; Wong-Staal F

Department of Medicine, University of California, San Diego, La Jolla

92093-0665, USA.

Journal of virology (UNITED STATES) Apr 1997, 71 (4) p3048-53,

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The chronicity of infection by the human immunodeficiency virus (HIV) calls for therapeutic regimens that offer sustained antiviral effects, such as gene therapy. Recent studies have demonstrated that expression of HIV mutant transdominant proteins, RNA decoys, and ribozymes efficiently inhibited HIV replication. We have previously shown that an RNA decoy (stem-loop II of the Rev response element of HIV type 1 [HIV-1], named SL2) and a ribozyme (Rz) targeting the U5 region of the HIV-1 5' long terminal repeat (LTR), combined in a fusion molecule, was more efficient in inhibiting HIV-1 replication than the ribozyme or the decoy alone. In this study, we expressed this fusion molecule in a retrovirus-based double-copy vector to obtain higher expression of this molecule. Furthermore, we inserted a sequence internally to drive expression of another fusion molecule with a ribozyme targeting the env/rev region linked to SL2 to obtain a triple-copy vector. These multigene antiviral vectors were subsequently transduced or transfected into human CD4+ T cells (Molt-4). Results showed that the translocation of the SL2-Rz cassette from the 3' to the 5' LTR occurred in 80% of the transduced cells. The numbers of ribozyme RNA transcripts, estimated by competitive-quantitative reverse transcription (RT)-PCR, were  $1.2 \times 10(5)$ ,  $1.2 \times 10(4)$ , and  $1.5 \times 10(3)$  copies per cell for the triple-copy, double-copy, and single-copy vectors, respectively. Cell challenge with multiple subtypes of HIV-1 (clades A to E) showed commensurate levels of virus inhibition for the three vectors. This study suggests that the combination of multiple anti-HIV genes, such

as ribozymes and decoys, targeting multiple sites of HIV RNA and expressed at high levels are promising for the treatment of HIV-1 infection.

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Evaluation of vaccines designed to induce protective cellular immunity against the Plasmodium yoelii circumsporozoite protein: vaccinia, pseudorabies, and Salmonella transformed with circumsporozoite gene.

Sedegah M; Beaudoin R L; Majarian W R; Cochran M D; Chiang C H; Sadoff J; Aggarwal A; Charoenvit Y; Hoffman S L

Infectious Diseases Department, Naval Medical Research Institute, Bethesda, MD 20814-5055.

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In an attempt to induce a protective cytotoxic T-cell mediated immunity against sporozoites of Plasmodium yoelii, the gene encoding the P. yoelii circumsporozoite (CS) protein was engineered into three live vectors: vaccinia, attenuated pseudorabies, and attenuated Salmonella typhimurium. Balb/c mice were immunized with 1-4 doses of  $10(8)$  pfu of the vaccinia construct (IP), 3 doses of  $10(5)$ ,  $10(6)$  or  $10(7)$  pfu of pseudorabies construct (IV), and 3 doses of  $10(9)$  salmonella transformants (orally). In the case of vaccinia and pseudorabies constructs, an excellent immune response was obtained as measured by antibodies to sporozoites. No protection or delay in prepatent period was seen in any of the experimental animals when challenged with 200 (vaccinia, pseudorabies) or 100 (salmonella) sporozoites, although mice immunized with irradiation-attenuated sporozoites were consistently protected against challenge with greater than  $10(4)$  sporozoites. Since other vaccinia, pseudorabies, and salmonella CS constructs have been shown to induce cytotoxic T lymphocytes (CTL) against the CS protein, it is likely that CTL against the CS protein were induced during these studies. It is currently unclear if the vaccines did not induce the appropriate CTL or inadequate numbers of CTL, or if CTL against the P. yoelii CS protein are inadequate to protect against sporozoite challenge.

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DIALOG(R)File 357:Derwent Biotech Res.

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Immunization with recombinant vaccinia viruses expressing structural and part of the nonstructural region of tick-borne encephalitis virus cDNA protect mice against lethal encephalitis - vaccinia virus vector-mediated tick-borne encephalitis virus gene expression in mouse for use as live recombinant vaccine (conference paper)  
AUTHOR: Dmitriev I P; Khromykh A A; Ignatyev G M; Gainullina M N; Ageenko V A; Dryga S A; Vorobyeva M S; Sandakchiev L S  
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CORPORATE SOURCE: Research institute of Molecular Biology, State Research Center of Virology and Biotechnology 'Vector', 633159 Koltsovo, Novosibirsk region, 633159 Russia.  
JOURNAL: J.Biotechnol. (44, 1-3, 97-103) 1996  
ISSN: 0168-1656 CODEN: JBTD4  
CONFERENCE PROCEEDINGS: New Approaches to Vaccine Development, NA VD'95 Symposium, Vienna, Austria, 11-14 April, 1995.  
LANGUAGE: English  
ABSTRACT: Three recombinant vaccinia virus vectors, which contained different fragments of the tick-borne encephalitis virus (TBEV) cDNA from the 5'-noncoding region to the end of the NS3 gene under the control of the native 7.5 k promoter, were constructed in order to establish the most immunogenic combination. Infection of CV-1 cells with the recombinant viruses vC-NS1 (coding for C-prM-E-MS1 region) and vC-NS3 (coding for C-prM-E-NS1-NS2A-NS2B-NS3) resulted in production of proteins identical in size to the TBEV E and NS1 proteins. However, cells infected with v5'C-NS2A (coding for the 5'-noncoding region and C-prM-E-NS1-NS2A regions) produced significantly less NS1 protein and very little if any of E protein. Immunization of mice with the vectors demonstrated that vC-NS3 induced high levels of TBEV-specific antibodies and protected them against i.p. challenge with 10 million LD50 of TBEV, while vectors vC-NS1 and v5'C-NS2A induced much lower antibody levels. This high level of protection with vaccinia virus vector vC-NS3 makes it a very attractive candidate for development of a live TBEV recombinant vaccine. (29 ref)  
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